HARVARD HEALTH TALKS, 9

REVISED EDITION

PNEUMONIA

BY

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Notable progress has been made in the study of pneumonia since the first edition of this book was published in 1922. Investigation has brought about a better understanding especially of the factors underlying recovery or death from the disease. Dr. Lord has therefore made a complete revision of the book, so that both the lay reader and the physician will find it a reliable, up-to-date discussion of the subject. In its new form it will doubtless continue to deserve the praise bestowed by *The Lancet:* "To those who have suffered many things from the usual type of popular lecture, this health talk will come as a happy relief."

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HARVARD HEALTH TALKS

PRESENTING the substance of some of the public lectures delivered at the Medical School of Harvard University, this series aims to provide in easily accessible form modern and authoritative information on medical subjects of general importance. The following committee, composed of members of the Faculty of Medicine, has editorial supervision of the volumes published:

PREFACE

NOTABLE progress has been made in the study of pneumonia since the first edition of this book. Important advances have added to the knowledge of the biologic peculiarities of the pneumococcus. The factors underlying recovery or death from the disease are better understood. Curative value in the early specific treatment of Type I pneumococcus pneumonia has been established by a comparison of the mortality in contemporaneous series of patients treated with and without anti-serum. Felton's success in refining antipneumococcus serum has made available a concentrated, potent, polyvalent antibody solution. This is more easily administered and is less likely to cause troublesome reaction than unrefined anti-serum. It has curative value not only against Type I, but probably also against Type II pneumococcus pneumonia.

PNEUMONIA

PNEUMONIA

REFERRING to pneumonia, Osler writes: "One of the most widespread and fatal of all acute diseases, pneumonia has become the 'Captain of the men of Death' to use the phrase applied by John Bunyan to consumption."

Frequency and Importance

In this country about 10 per cent of all deaths are each year due to some form of pneumonia and this annual toll of lives has been maintained with little apparent variation for many years. Strictly comparable statistics are lacking for other communities but, making due allowance for differences in classification, a similar high prevalence seems to obtain also in other civilized countries in which mortality statistics are available.

While the disease is constantly a menace and thus termed endemic, numerous instances might be cited of more or less severe local outbreaks or epidemics at certain times and in certain places as a succession of cases in the same house, on shipboard, in hospitals and in jails. Conditions of overcrowding are largely responsible for such epidemics. In 1906 the death rate among negroes employed in the construction of the Panama Canal reached eighteen per thousand. A similar high mortality has been noted among negroes employed in the mines on the Rand and in 1912 the death rate from pneumonia was twenty-six per thousand. In Panama and on the Rand the highest mortality occurred among the recent arrivals and the mortality rapidly diminished after a short residence in the community.

We passed through a period of greatly increased prevalence of pneumonia during and after the influenza pandemic. In

the absence of reliable figures it is futile to speculate as to the number of deaths from pneumonia in the country at large during the scourge of influenza; but the importance of pneumonia as a cause of death is strikingly illustrated in the report of Vaughan and Palmer for the United States Army during the World War. Of about 4,000,000 men, about 40,000 perished in combat and 47,000 died from disease. Pneumonia accounted for more than 50 per cent of the deaths from disease prior to the influenza pandemic in 1918 and for 93.7 per cent during the period covered by the pandemic. Men from the rural districts and the southern communities suffered most severely. Excluding the influenza period from consideration, pneumonia was nine times more frequent among the men in the army than among civilians of the same age group. The high incidence of pneumonia in the army may be ascribed to epidemics of measles and

influenza followed by pneumonia, an increased opportunity for contagion in the close proximity of susceptible individuals in barracks, tents, and the mess, and a lowering of resistance from exposure, overwork, and fatigue.

Types of Pneumonia

I have thus far spoken of pneumonia without distinction as to type, and before proceeding further it will be necessary to define the two recognized forms of the disease; one is spoken of as *lobar pneumonia* from the more or less complete involvement of one or more lobes of the lung in an inflammatory process. In this type there is practically always one group of bacteria, called pneumococci, to be found in the lung and frequently also in the blood. Lobar pneumonia is a disease with a well-defined and uniform onset, usually with initial chill, rapid elevation of temperature, pain in the side, cough and bloody

expectoration, running a febrile course of about seven days and terminating abruptly in favorable cases. The second type is known as *bronchopneumonia* and here the bronchi or smaller air passages and even their smallest ramifications in the lungs together with the adjacent or terminal air vesicles and the neighboring lung are the site of an inflammation. In bronchopneumonia the infecting agents are usually micro-organisms normally inhabiting the mouth, and hence the bacterial flora in the mouth of normal persons to a considerable degree determines the bacteriology of the disease. The pneumococcus is the most common single cause but other organisms are also concerned and mixed infections with more than one kind of bacteria are not uncommon. In contrast to the usual, well-defined and uniform onset and abrupt termination of the symptoms in lobar pneumonia, bronchopneumonia presents a variable pic-

ture, occurring as a complication of conditions likely to mask or modify its manifestations and with a variable extent of lung involvement.

Causes

In considering the causes of pneumonia, it is desirable to distinguish between the predisposing and immediate causes. Among the *predisposing causes* susceptibility is increased as age advances. It is greater among males than females, probably on account of greater opportunity for infection in occupations among males. The subjects of chronic alcoholism are somewhat more prone to pneumonia as suggested by an apparent higher percentage of heavy drinkers in patients admitted to hospitals with pneumonia than in the other patients and in the population at large.

There is a marked seasonal variation in the incidence of pneumonia, a large majority of the cases occurring during

the months between November and June. The explanation is uncertain but the tendency to live under less satisfactory hygienic conditions in crowded and poorly ventilated rooms during cold and inclement weather may be responsible. A greater incidence of pneumonia in the city than in the country suggests that overcrowding is a factor of importance. Close contact within doors increases the opportunity for transmission of infectious material from one person to another through the distribution of particles by loud talking, coughing, and sneezing in houses, theatres, halls, barracks, street cars, etc., and contamination by fingers soiled with saliva or sputum.

The increased susceptibility of recent arrivals in a community, as in the United States Army, in Panama, and on the Rand, may be ascribed to less previous exposure and consequently less acquired resistance to organisms which abound in crowded communities. Such debilitating

conditions as hunger, fatigue, exposure to wet and cold, the later stages of cardiac disease with passive congestion of the lung, malignant disease, chronic nephritis and cerebral hemorrhage are also to be regarded as predisposing factors.

A history of acute infection such as accompanies an ordinary "cold" can be obtained in from 25 to 50 per cent of all cases of lobar pneumonia and such infections may be regarded as important predisposing factors, the specific agent of the "cold" (as yet unknown) probably acting to carry down the cause of pneumonia into the deeper parts of the respiratory tract and leading to its implantation in the lung. Measles, influenza, and whooping cough are also not infrequently followed by pneumonia, more often of the bronchopneumonic type. In these three diseases the specific cause probably acts in similar fashion to implant the pneumococcus within the deeper parts of the tract.

Bacterial cause of pneumonia. The pneumococcus is practically the only *immediate* cause of lobar pneumonia and the most common single cause of bronchopneumonia. Our knowledge of the organism extends over a period of nearly fifty years and goes back to its independent and almost simultaneous discovery by Sternberg in September and by Pasteur in December, 1880. Unfortunately for American medicine, Sternberg's article did not appear until April, while Pasteur's publication is dated January, 1881, and the priority of the discovery therefore belongs to Pasteur. The importance of the pneumococcus, however, was not appreciated until its frequent presence in pneumonia was established by Fraenkel in 1884 and later by Weichselbaum in 1886. It is a lance-shaped organism occurring in pairs or chains and is found in the saliva of more than one half of all normal persons.

Types of Pneumococci

Previous to the work of Neufeld (Arb. a. d. Kais. Gesund. 1910, xxxiv, 293) in Germany and of Dochez and Gillespie (Journal Am. Med. Ass., Sept. 6, 1913, lxi, 727) in this country, it was thought that there was no essential difference in the strains of pneumococci. By the repeated inoculation of horses with different strains it has been found, however, that after a time the animal's resistance against the organisms injected is such that when its blood is taken and allowed to separate into serum and clot, the serum will protect white mice against an otherwise fatal dose of certain strains of pneumococci. The increased resistance of the horse in consequence of the inoculations is spoken of as an acquired immunity and the elements in the immune horse serum responsible for the increased resistance are known as protective substances or antibodies. The immune horse serum is not only protective

but will also cure an otherwise fatal infection. It is further found that those strains against which the horse serum is effective can be recognized by a clumping or agglutination of the pneumococci when mixed in suspension with the horse serum. By such protective and clumping experiments three so-called "fixed" types of organisms have been separated out of the great group of pneumococci. In the first column (A) of Table I (page 23) the groups are indicated by the Roman numerals. The types numbered I, II, and III are the fixed types. Type IV is made up of pneumococci with individual characters and resistance against one strain of this type confers no protection against other strains. It is thus spoken of as a heterogeneous group. As shown in the second column (B) Types I and II are only rarely present in the normal mouth, while Types III and IV are common. Among persons intimately associated with pa-

tients with lobar pneumonia, however, such as attendants, relatives or friends, the percentage of those who harbor Type I or II pneumococci may rise as high as 13.0 per cent. (Avery, Chickering, Cole, and Dochez. Monographs of the Rockefeller Institute for Medical Research, No. 7, October 16, 1917, p. 95.)

Relation of types of pneumococci to types of pneumonia. I cannot give you data on the incidence of the different types in bronchopneumonia but their approximate frequency is indicated by the plus signs in the column (C). As in the saliva of normal persons Type IV is most common, Type III is probably next in frequency and Types II and I are rarely present. I would like to point out also that the similar grouping in the saliva of normal persons and in bronchopneumonia is what we should expect, as the infection here is usually due to bacteria commonly inhabiting the mouth

TABLE I. — INCIDENCE OF TYPES OF PNEUMOCOCCI IN THE NORMAL MOUTH AND IN THE SPUTUM OF CASES OF BRONCHOPNEUMONIA AND LOBAR PNEUMONIA

	Human Beings			
A	B	C	D	E
Types of pneumococci	Incidence in normal mouth [1]	Incidence in broncho-pneumonia	Incidence in 1918 cases of lobar pneumonia [2]	Lobar pneumonia. Outcome in 1107 cases not serum treated. Percentage of deaths in each group [2]
I	0.8%	+	33.6%	20.7%
II	0.0%	+	19.1%	42.0%
II atypical	18.2%	++	....	....
III	28.1%	+++	13.3%	41.6%
IV	52.9%	++++	33.1%	29.2%

[1] Avery, Chickering, Cole and Dochez, Acute Lobar Pneumonia, Prevention and Serum Treatment. Monograph of the Rockefeller Institute for Medical Research, No. 7, October 16, 1917.

[2] Cecil, Baldwin and Larsen, Arch. Int. Med., Sept., 1927.

and carried down into the deeper parts of the respiratory tract.

The distribution of types in 1913 cases of lobar pneumonia, determined by Cecil, Baldwin and Larsen is shown in the fourth column (D). Out of every 100 cases about thirty-three are due to infection with Type I, about nineteen to Type II, about thirteen to Type III and about thirty-three to Type IV. The low incidence of Type I and II in the normal mouth and their incidence, in about 50 per cent in cases of lobar pneumonia, is in accord with the behavior of other disease-producing bacteria, such for example as the diphtheria bacillus which may be harbored by a small proportion of normal persons without giving rise to the disease diphtheria. The limitation of Type I and II to patients with lobar pneumonia and to those in contact with such patients suggests that pneumonia due to these two types of pneumococci is largely acquired by contact with pa-

tients with or recently recovered from pneumonia, or by contact with a healthy carrier who has been exposed to a patient with pneumonia. Pneumonia due to Type I and II pneumococci is thus to be regarded as a communicable disease and such a consideration makes it desirable to isolate patients with lobar pneumonia and thus protect other persons so far as possible. Type III and Type IV lobar pneumonias, which together represent about 50 per cent of the cases, may be regarded as due to auto-infection from organisms normally inhabiting the mouth, but increased virulence of these pneumococci or diminished resistance of the host may also be of importance in giving rise to pneumonia.

Biologic Peculiarities of Pneumococci

The pneumococcus has interesting biologic peculiarities which are doubtless concerned in its behavior as an infecting

agent. It is very sensitive to environmental conditions and when grown in unfavorable culture media loses its capacity to form capsules, its virulence and is more readily taken up and killed by the white cells of the blood or leucocytes. These remarkable changes may be induced by growth of the organism in serum obtained from animals immunized against the pneumococcus. By one or more passages of such changed organisms through a susceptible animal, as the mouse, these changed organisms, called by Griffith R pneumococci on account of the rough surface of their colonies, can be reconverted into type specific and virulent organisms known as S pneumococci on account of the smooth surface of their colonies.

It is important to determine whether such a change from S to R pneumococci takes place in, as well as outside, the body. Wadsworth and Sicles have found that the pneumococcus multiplying in

the tissues of the immune horse loses in varying degree its capacity to form capsules, its type specificity and virulence and that in some instances the typical pneumococcus characteristics could be quickly restored by passage through animals. Reiman has also shown that a change from S to R forms takes place in the blood stream of infected horses, but a complete change of all organisms from S to R pneumococci could not be demonstrated.

The bearing of these observations on the explanation of recovery from pneumococcus infection is at present doubtful. They suggest the possibility that under the influence of protective antibodies or other unknown influence in the living tissue fluids, virulent S forms may be changed into avirulent R forms and the subsequent destruction of the latter may take place by the action of the white cells of the blood.

The pneumococcus has other interest-

ing biologic peculiarities which may be concerned in its behavior as an infective agent. It is very sensitive to a change in the reaction of the media in which it grows and growth can be started in artificial media only at a reaction very close to that of the circulating blood which is slightly alkaline. In artificial media containing carbohydrate such as glucose, however, growth, once started at a slightly alkaline reaction, proceeds until the media become slightly acid, further multiplication being inhibited by the acid produced. Its extreme sensitiveness to acid may be better appreciated when it is stated that the range between the slightly alkaline reaction of normal blood and that of the culture containing glucose in which death of the organism takes place is about that between ordinary tap water and distilled water standing in the laboratory.

The lower animals vary in their susceptibility to infection with the pneu-

mococcus, chickens and pigeons being immune, and rabbits, rats, and mice highly susceptible. The readiness with which artificial infection of these lower animals can be produced in the laboratory has led to important additions to our knowledge of the organism and an advance in treatment of the disease with consequent reduction of mortality.

"Crisis" in Pneumonia

I have already referred to the abrupt termination of lobar pneumonia in favorable cases. This turn of events in the disease is spoken of as "crisis" and some apprehension is naturally felt by anxious relatives when this term is used, but when crisis occurs in pneumonia it is usually a favorable event, during which the temperature falls to normal without any accompanying emergency and within twelve to twenty-four hours there is a rapid transition from a condition of great gravity to one of safety. The crisis

is usually an indication of a decisive victory won by the patient against the disease.

Factors Underlying Crisis and Recovery. The determination of the factors underlying crisis and recovery from lobar pneumonia is one of the most interesting fields for research. Much valuable information has already been won but there is still much to be learned. A complete explanation may be expected to open the way to still further advance in treatment. Our present conception is that recovery is a dual mechanism, on the one hand chiefly dependent on the development of a general resistance against the pneumococcus during the course of the disease and on the other certain chemical changes in the involved lung itself leading to death of the organism.

There is considerable evidence in favor of the development of a general resistance during the short period from the

onset to the termination of the pneumonia. The evidence is at first sight apparently paradoxical because of the frequency with which recurrent attacks of pneumonia may occur in the same individual. This may be due, however, to the fact that the resistance acquired by one attack is sufficient to terminate that attack without affecting any lasting protection. The additions to our knowledge of the different types of pneumococci suggest another and more plausible explanation. I have already referred to the increase of resistance in horses following repeated injections of different strains as a means of recognizing the fixed types of pneumococci. By such injections rabbits as well as horses can be rendered highly immune against many times the otherwise fatal dose of pneumococci of Type I, II, or III. The resistance thus artificially induced, however, is protective only against the same type of pneumococci as that used in the injection and

not against any other type. While occasional instances of Type I, II, or III pneumonia in man are known to have been followed by a second attack due to the same type as that concerned in the first infection, the repetition is usually due to pneumococci of another type, suggesting that in man an immunity may be induced against one but not against another type. Other evidence is also confirmatory in man of the building up of resistance against the particular type giving rise to the pneumonia. Blood from patients with Type I, II, or III pneumonia obtained at about the time of crisis and injected into animals has the power of protecting them against an otherwise fatal dose of the same type of pneumococci. It is ineffective in protective power against any other than the same type, indicating a specific response on the part of the individual against the particular type giving rise to the infection but not against any other type.

Recovery or death in pneumonia is chiefly to be ascribed to a balance between these protective substances produced by the infected individual on the one hand, and inhibiting substances emanating from the invading organism on the other. The mechanism by which these opposing forces work is not wholly understood. Protective substances have not been isolated in a pure state and are recognized only by their action. They are known to inhibit growth of pneumococci and favor their destruction by the white cells of the blood. Baldwin and Cecil (J. A. M. A. Nov. 20, 1926) in an investigation of 25 patients at various intervals during the course of the disease found that in 12 protective substances could be demonstrated at least two days before the crisis and in 8 at or just after the crisis. In 5 no protective substances were found at any time during the course of the infection. Of the 20 patients with protective substances at

some time during the course of the disease 3 (15 per cent) died while of 5 without protective substances all died.

The presence of protective substances in the blood is to be regarded as of favorable import, but it is too much to expect that a positive balance of protection in the blood will always indicate that the patient will recover. The presence of protective substances may be taken to mean that the defenses of the host against the invading organisms have for the time being the upper hand, but the patient may, nevertheless, succumb exhausted by the struggle. The absence of protective substances on the other hand may be looked upon as unfavorable.

It is important in the solution of the pneumonia problem to know more about these protective substances and especially their relation in large series of cases to recovery. It seems clear, at present, that they are of chief importance in the outlook, and if it should be found that

practically all patients with protective substances in the blood recover and practically all those without such substances die, it would eliminate the possibility which must at present be entertained that there may be other factors concerned in the explanation of crisis. The investigation of this matter is performed by the estimation in mice of the degree of protection, if any, which is afforded against otherwise fatal doses of pneumococci by the patient's serum. The investigation is time consuming and expensive on account of the number of mice required for the tests in the study of each patient with pneumonia.

In patients with Type I and Type II pneumococcus pneumonia, it is possible to maintain a positive balance of protective substances in the blood by the use of Felton's antibody solution (Baldwin and Cecil, Park and Cooper) about which more will be said later.

Mention has already been made of

inhibiting substances emanating from the pneumococci. These inhibiting substances as factors of importance in the struggle between the invading organism and the host are in themselves non-toxic, but favor the mastery of the host by the organisms from their property of neutralizing or destroying protective antibodies and enhancing the virulence of the organism. These inhibiting substances are formed in greater amount as the infection proceeds and hence better results may be expected from early than late specific therapy.

Local chemical factors may also be concerned in recovery but their influence is thus far hypothetical. Mention has already been made of the susceptibility of the pneumococcus to changes of reaction in the media in which it grows and of its rapid death in the presence of a slight degree of acidity. As the inflammatory process in the lung goes through its evolution two significant changes take place

in the involved region. The amount of blood diminishes and the reaction, so far as we can learn from animal experiment and tests of the lung immediately after death, changes from slightly alkaline to a degree of acidity within the range of the acid death point of the pneumococcus. In the study of these factors we have found that there is an important relation between the amount of blood serum and the effect of acidity on the pneumococcus, serum protecting the organism to a certain extent from degrees of acidity which would otherwise kill it. At an acidity corresponding to that which the inflammatory process may reach, however, the duration of life of the pneumococcus in fluid culture media without serum is only about two hours and even 100 per cent serum may not suffice to prolong the life of the culture for more than twenty-four hours. In explanation of the factors contributing to recovery from a chemical point of

view it may be conceived that as the evolution of the local process takes place with an increase of acidity and diminishing amount of serum the acid death point of the pneumococcus is reached. The favorable effect of a positive balance of antibodies may be supplemented by this chemical change in the lung and crisis and recovery follow.

Resolution

Another interesting aspect of lobar pneumonia is a most remarkable change which takes place in the inflammatory process in the lung. In consequence of infection with the pneumococcus the affected region becomes firm and solid from the presence everywhere within the smallest air spaces of great numbers of cells technically known as polymorphonuclear leucocytes or pus cells and a fine network of delicate threads which permeate the whole structure. These are threads of fibrin and you are all

familiar with an important result of their presence in shed blood which they cause to coagulate or clot shortly after its escape from the blood vessels. At the same time with or shortly after the crisis this solid lung begins to soften, sooner or later air again enters the region and finally in spite of the profound inflammatory changes through which it has passed it is restored to the functional capacity existing before the pneumonia, no trace of which now remains. This extraordinary transformation is spoken of as resolution.

Factors Underlying Resolution. That resolution can occur without permanent damage to the lung itself is due to the fact that the products of the inflammatory process are poured out into the air spaces with little involvement of the framework of the lung itself in which the circulation of blood, though impaired, is still maintained. The softening of the exudate without damage to the lung

tissue is accomplished by three interesting and delicately balanced factors.

The principal agent in the transformation is a peculiar substance liberated by the pus cells which have migrated to the air spaces and form part of the inflammatory process. This remarkable substance is known as an enzyme (or ferment). If you are not already familiar with the fundamental importance of enzymatic action in and outside the body, I may emphasize it by saying that to enzymatic action is to be ascribed the ripening of fruit, the tenderness and taste of meat, the alcoholic fermentation of sugar by the yeast cell, the digestion of food in the stomach and intestines and in fact the chemical activity of all living plant or animal cells. Ferment action in the body is a powerful force for good but must be prevented from doing harm by some regulatory mechanism. Two protective factors hold it in check in the

body. Enzymatic action is inhibited by the blood serum and does not take place when there is an abundance of blood. The action of enzymes is largely dependent also upon the reaction of the medium in which the enzyme occurs. Thus the enzyme of the gastric juice works best in a strongly acid medium. Two enzymes are demonstrable in the pneumonic lung, one active in slightly alkaline, neutral, and slightly acid media and another with optimum activity in still more acid media. As the evolution of the pneumonic process takes place there is an increase in cells containing ferment, a diminution of serum containing antiferment, and a shift to an acid reaction. In the balance between cellular material and serum, enzymatic action is absent with more and present with less than about three parts serum to one part cells. Increase of cells (enzyme), diminution of serum (antienzyme), and a shift

to an acid reaction thus permit the melting away of the exudate and restoration to normal.

Diagnosis of Pneumonia

In typical cases the diagnosis of lobar pneumonia is readily made from the history of an acute onset with chill, rapid rise of temperature, pain in the side, cough with bloody expectoration and shortness of breath, and on examination the signs of consolidation in the lung. The usual occurrence of bronchopneumonia as a complication of some infection of the upper respiratory tract, the insidious onset, irregular course and frequent absence of definite physical signs make the diagnosis of bronchopneumonia difficult and at times impossible. In fact, it often happens that the diagnosis of bronchopneumonia can only be regarded for a time as probable from the attendant circumstances, the symptoms, and the physical signs. Into the

more technical aspects of the diagnosis it is not necessary for me to go.

Diagnosis of the Type of Pneumococci

The use of a refined antiserum (Felton's antibody solution) now makes it possible to begin treatment of patients with pneumonia regardless of type, but it is still desirable that the type of infection be determined at the earliest possible moment.

Inasmuch as there are no clinical features which serve to distinguish the different types of pneumococcus infection one from another, resort must be made to the laboratory. The evolution and grouping of initial symptoms of lobar pneumonia are so striking that the first specimen of sputum obtainable should be sent at once to the laboratory for the determination of type. The sputum should come from the deeper parts of the air passages. It should be collected in a

small, wide-mouthed, clean and preferably sterile bottle. As the determination of type usually depends on the presence of living organisms in the sputum no antiseptic should be added to the specimen. In the laboratory a part of the specimen is examined under the microscope and a small amount injected into the abdominal cavity of a mouse. Virulent pneumococci multiply rapidly in the mouse and on removal of the abdominal fluid their type can be determined by mixing pneumococci thus obtained or small amounts of the abdominal fluid with sera obtained from horses each immunized with Type I, II, or III pneumococcus. A correspondence of the organism giving rise to the pneumonia to one of these types is indicated by a clumping or precipitation when mixed with the corresponding serum. A diagnosis of type can thus be made usually within eight to twenty-four hours. If large amounts, two to three teaspoon-

fuls, of sputum can be obtained a rapid precipitation method may permit of a determination of type within a few minutes. The type of infection can also at times be determined by blood culture. The State Board of Health of Massachusetts determines the type without charge.

Prognosis

The outlook for life in lobar pneumonia depends upon many factors, all of which cannot be considered. In general it may be said that the mortality in pneumonia is about 25 per cent. This figure represents the mortality in general hospitals where the poorer classes are admitted. Diminished resistance from poor nutrition, overwork, fatigue, and chronic alcoholism makes the death rate somewhat higher in hospitals than may be expected in private practice where the mortality may be 20 per cent or less. Of the various factors influencing the

outcome age is of much importance. Youth is favorable. From the sixth to the twentieth year the mortality is not far from 6 per cent. It rises steadily as age advances reaching about 26 per cent from thirty-one to forty, nearly 40 per cent from forty-one to fifty and may rise as high as 65 per cent above sixty years of age. The mortality varies also according to the type of pneumococci giving rise to the infection. As shown in Table I Column E about 20 per cent of the cases due to Type I and about 40 per cent of Type II are fatal. About 40 per cent of patients succumb to Type III pneumonia and about 30 per cent to Type IV. The influence of treatment with Type I serum in lowering the mortality of Type I pneumococcus pneumonia will be considered later.

Prevention

I want next to call your attention to certain aspects of prevention of pneu-

monia. This is a difficult matter and our limitations must be at once acknowledged. The high incidence of pneumonia in the army camps and the scourge of post-influenza pneumonia which swept the country in the fall of 1918 indicate that we have much to learn regarding prevention. Indeed it would almost seem from the undiminished death rate from pneumonia over long periods of years that our efforts are thus far wholly unavailing.

There are three principal means of attack upon the prevalence of the disease, one already available, the others promising for the future.

The method already available is the application to pneumonia of such knowledge as we already possess regarding the transfer of infectious material from person to person in communicable disease and there is this hopeful aspect for the future, that such transfer has not been adequately avoided in the past. The

more recent knowledge acquired regarding the distribution of types of pneumococci in health and disease suggests that pneumonia due to Type I and Type II pneumococci arises from direct contact with patients with pneumonia or from contact with healthy carriers who harbor these organisms in consequence of exposure to lobar pneumonia. As Type III and Type IV pneumococci commonly inhabit the mouths of normal persons, however, the indication is less clear regarding the prevention of pneumonia due to these types. We know, however, that passage of bacteria through susceptible animals increases their virulence and transfer of pneumococci of whatever type from patients with pneumonia to those about them doubtless favors the development of pneumonia.

These considerations are an incentive to greatly increased caution and make isolation and quarantine of patients with

pneumonia desirable to guard against the transfer of disease-producing pneumococci from person to person. Transfer may take place by contact with moist sputum or utensils used by infected individuals. It may also occur by what is known as droplet infection through the inhalation of particles of moist sputum expelled by talking, coughing, or sneezing, or by the inhalation of material which through drying may contaminate the air. Medical cleanliness, in the sense of freedom from the danger of bacterial infection, must be secured in the sick room. The sputum should be expectorated into a special receptacle and this should be burned. Drying should be prevented by avoidance of long standing. Droplet infection may be avoided by placing a piece of cloth in front of the mouth during coughing or sneezing, and the cloth should be burned. Patients with pneumonia should be isolated to guard others

against contact, droplet and dust infection. Those in attendance should wash the hands before eating in order not to carry infectious material to the mouth. The soiling of bedding or clothing should be avoided. Soiled material should be removed, handled without shaking, and sterilized. Dry sweeping or dusting of the sick room should not be permitted. Eating utensils should be kept separate and sterilized. The room vacated by a patient with pneumonia should be thoroughly cleaned and disinfected. Sunlight limits the danger of the persistence of living pneumococci in the room.

These suggestions apply to the care of the sick room. Attention must also be paid to measures to limit the spread of infectious material by the public at large. The regulations of the Board of Health forbidding expectoration in public places should be more strictly enforced. Contamination by turning the leaves of books and public documents

after moistening the finger in the mouth should be avoided.

It should be recognized that overcrowding greatly increases the danger of transfer from person to person. A factor of great importance in the army was the increased opportunity for contagion in the close contact of susceptible individuals in barracks, tents, and the mess. Such crowding is a serious menace and responsible for the loss of many lives. Though unavoidable in the face of a national emergency, the danger may be diminished by head to foot sleeping, screening by the cubicle system, and separation by screens at mess. The bedding and barracks should be thoroughly cleaned and aired. Overcrowding is to be avoided in civil as well as military life and an improvement of housing conditions in our cities will diminish contact infection. As dust is concerned in the spread of respiratory infections, the amount of city dust and smoke should be

diminished. When in any community respiratory infection reaches a menacing prevalence, mass meetings should be forbidden, schools should be closed, and infected boats should not land passengers at uninfected ports.

There are certain precautions which apply particularly to the individual. Infection with organisms normally harbored in the mouth is responsible for about 50 per cent of the lobar pneumonias and for a large proportion of the bronchopneumonias. Persons with an infection of the respiratory tract such as accompanies a "cold," influenza, tonsillitis, etc., should avoid chilling of the body, exposure to draught when insufficiently clad, and rapid cooling when overheated. The danger of inhalation of infectious material may be diminished by breathing pure air free from dust, the maintainance of an equable temperature in the house, and careful cleaning of the teeth and mouth during the fevers and

preceding any operative procedure under a general anesthetic. Operations under general anesthesia should be avoided in other than emergency cases during any nasal infection, tonsillitis, or cough, and the operation postponed until the infection has wholly subsided. In the presence of such an infection, an imperative operation should if possible be done under local rather than general anesthesia, or if general anesthesia must be used, gas-oxygen is to be preferrred to ether.

Still another matter of importance is the recognition that there is to a certain degree a predisposition to pneumonia in the lowering of resistance by inadequate food, exposure, overwork and fatigue, and greater attention should therefore be paid to enough and proper food, sufficient clothing, and a suitable balancing of activity and rest.

Preventive measures must, however, go further than this and strike more

nearly at the root of the pneumonia problem and this brings us to the first of the two methods of attack with promise for the future. Such diseases as measles, whooping cough, influenza, and diphtheria in which there is an infection of the upper parts of the respiratory tract are prone to be complicated or followed by pneumonia, usually of the bronchopneumonia type. To eliminate pneumonia secondary to these diseases, the diseases themselves must be brought under control. More adequate isolation than is now customary will diminish the frequency of measles, whooping cough, and influenza, but further investigation of the causative agents and a better understanding of the mode of transmission are necessary preliminaries to complete success. It is highly important that the public recognize our deficiencies in these matters, and demand and financially support further investigations for the solution of the problem.

Regarding diphtheria it may be said that the brilliant researches of the past few years have made the disease entirely preventable. To have it will in the future be a reproach to the intelligence or the enterprise of a community. Not all persons are susceptible to diphtheria. A simple, safe, and reliable test, known as the Shick test, will determine the susceptible individuals who can then be made immune, by the injection of a diphtheria toxin-antitoxin mixture. The State Department of Health of Massachusetts furnishes to physicians the materials for testing susceptibility and immunization against the disease.

There is one other hopeful prospect of success in the prevention of pneumonia. Typhoid fever and small pox, once the scourge of armies, have practically disappeared as the result of preventive inoculation and it was natural to expect that the application of similar methods might diminish the incidence of pneu-

monia. Successful immunization against typhoid fever is accomplished by the injection under the skin of a suspension of dead typhoid bacilli. By the injection of animals with dead pneumococci of any type, a considerable degree of resistance to virulent pneumococci can be obtained. But for the production of the highest grade of resistance in animals it is necessary to inoculate the animal with living cultures.

Preventive inoculation against pneumonia by means of a pneumococcus vaccine was first attempted on a large scale by Wright among the miners in South Africa. The experience at the Premier Mine in 1913 was promising. Among seventeen thousand inoculated the death rate from pneumonia was six per thousand while among six thousand seven hundred uninoculated the death rate was seventeen per thousand. By the use of a vaccine containing types of pneumococci prevalent in the mines, Lister

later found that no cases of pneumonia of the type against which the men had been vaccinated developed during nine months of observation. Cecil and Austin at Camp Upton and Cecil and Vaughan at Camp Wheeler obtained encouraging though inconclusive results on soldiers during the World War. Cecil and Blake found that the inoculation of monkeys with dead pneumococci failed to protect them against experimental pneumonia though it lessened the mortality from the disease. For protection it was necessary to inoculate monkeys not with dead but with living pneumococci. I mention these matters to acquaint you with the problem, which is difficult for the prevention of human infection and must still be regarded as in the experimental stage. Thus far there is not sufficient evidence to justify the general adoption of preventive inoculation against pneumonia, but it may be used to protect individuals subject to recurring attacks. The im-

munity thus obtained probably lasts less than a year.

Treatment

In discussing the treatment of pneumonia it will be most convenient to speak first of general measures and later of specific therapy.

General Measures of Treatment. — Whether the patient should be treated at home or in a hospital depends largely upon the financial resources of the family. If proper medical oversight and nursing cannot be obtained at home it is better for the patient to be moved to a hospital. The decision, however, should be reached early in the disease when the patient can stand the journey without undue fatigue and the transfer should be made with the patient lying down.

Every effort should be made to conserve the patient's strength and resistance by rest, proper feeding, and fresh air. The elimination of toxic material

may be favored by an abundance of water. The patient should be absolutely at rest in bed and not allowed to sit up, moved and not allowed to move himself. In the course of pneumonia there is at times a plugging of the bronchi with consequent absorption of air and the trapping of infectious material in that part of the lung supplied by the occluded passage. This undesirable complication is prone to occur in patients who are allowed to lie constantly on one side. It can to some extent be avoided by turning the patient frequently from the back to one or the other side during the course of the disease. He should be fed and not permitted to feed himself. During the feeding he should remain recumbent, and liquid nourishment may be taken through a bent glass tube. There are no special indications regarding diet and the patient may take as much of simple and nutritious food as he can digest. During the early stages of the disease

the diet usually consists of milk and milk preparations, orange juice, broth and albumen water, with a more liberal diet as the fever subsides and the appetite returns. If the bowels have not moved a mild cathartic may be given at the outset. If abdominal distention from gas is troublesome or if there is vomiting, all food may be stopped for a time. If necessary a daily suds enema should be given. The room should be well lighted and well ventilated and the windows thrown open to secure an abundance of fresh air. Keeping the patient out-of-doors in cold weather is unnecessary, but facilities for moving the patient into a porch adjoining the room are desirable.

Patients with pneumonia should never be left alone on account of the danger of sudden and unexpected delirium which may lead to injury or accident.

Drugs and Other Non-Specific Measures. Are there drugs or other measures

of value in treatment? Various special methods of treatment have been tried at different times and in different places. Without going into the matter in detail, it may be said that with one exception the infection is beyond our control other than by such measures as tend to spare and support the strength of the patient by careful nursing and the alleviation of symptoms. Even by these simple means lives may be saved, more particularly in those cases in which there is a balancing between life and death, and the utmost care may turn the scale in the right directions. Special diets, drugs of various kinds, including alcohol, hydrotherapy, and venesection, have not been shown to influence the course and outcome of the disease. But morphia is of great value in relieving the pain in the side which otherwise prevents sleep, aggravates the shortness of breath, and harasses and fatigues the patient. It relieves the pain, conserves the patient's

strength, and may thus enable him better to withstand the infection. Digitalis, a drug with special action on the heart, may be of value especially in cases where there is irregularity of the heart with fibrillation of the auricles. There is promise in the course of time of the development of a specific drug therapy. A derivative of quinine known as "optochin," discovered by Morgenroth, has been shown by experiments in animals to protect against subsequent infection and cure an otherwise fatal infection with pneumococci, but large enough doses to be effective in man are too dangerous to use and it cannot be recommended. Its discovery, however, is of great importance, as it is the first chemical agent definitely shown to have a bactericidal effect in the living body. Its discovery is a great incentive to further investigation.

Specific Serum Treatment of Pneumonia. In discussing the factors under-

lying crisis in pneumonia attention was called to the specific protective and curative action in animals of the serum of horses immunized against the different types of pneumococci.

Results of Specific Treatment in Animals. Preventive and curative action of such immune serum is readily demonstrated in laboratory animals against otherwise fatal doses of Type I, II and III pneumococci.

Goodner (J. Exp. Med., July 1 and Sept. 1, 1928) has found that the injection of Type I pneumococcus into the skin of rabbits produces a local inflammation, invasion of the blood stream by pneumococci and death in a majority of the animals. This symptom complex is in many respects analogous to that in human lobar pneumonia. In about fourteen per cent of the rabbits there is spontaneous recovery with a critical fall in the temperature and the appearance of protective substances in the blood.

Prompt recovery can be brought about by the intravenous administration of Type I antipneumococcic serum. The necessary amount of serum increases very rapidly as the disease progresses.

Successful results have been obtained in monkeys with experimental pneumococcus pneumonia by Cecil and Blake (J. Exp. Med. 1920, Vol. 32, 1) Cecil and Steffen (Bull. 141, Hyg. Lab. U. S. P. H. S. 1924) and Baldwin and Cecil (J. A. M. A. Nov. 20, 1926). Owing to the close phylogenetic relation of monkeys to man, their results suggest that there is therapeutic value in Type I and probable value in Type II antipneumococcic serum in human patients with Type I and Type II pneumococcus pneumonia.

To judge from the experiments in animals early adequate dosage is of extreme importance in checking invasion of the blood stream by pneumococci and promoting recovery.

Development of Specific Treatment for Man. The earliest experiments, indicating that laboratory animals could be rendered immune to otherwise fatal doses of pneumococci by the previous injection of dead or sublethal doses of living pneumococci and that the serum of such animals possessed protective and curative action, led to the trial of immune serum in the treatment of man. The subcutaneous inoculation of small amounts of immune horse serum in patients with pneumonia gave inconclusive results. During this early period, the differences between the various strains of pneumococci was unknown. After the recognition of different strains of pneumococci it was found that the repeated inoculation of animals with a strain of any one of the three fixed types, I, II, and III, led to the development of an immunity specific for the type used and the serum of the animal thus immunized was found to have protective and cura-

tive action only against the homologous organism.

For the development of methods and the application of the principles of serum therapy to human infection, we are indebted to Dr. Rufus Cole and his associates at the Hospital of the Rockefeller Institute. It was at first thought that a sufficiently potent antiserum for the treatment of man could be obtained in horses only for Type I pneumococcus pneumonia and that in consequence, serum treatment was applicable only to that type. Moreover, the serum was found effective only in large doses given intravenously. To avoid the ineffectual use of large amounts of alien serum in patients with other than Type I infection, it was necessary to determine the type before the serum was used.

Felton (Boston Medical and Surgical Journal, May 15, 1924) of the Harvard Medical School in 1924 found by the simple expedient of diluting antipneu-

mococcic serum with water that from the resulting precipitate a concentrated antibody solution containing only small amounts of the protein of horse serum could be made. This concentrated solution retards the growth, promotes the killing of pneumococci by the white blood cells of the body and decreases the virulence of the organism. Felton's antibody solution is effective not only against Type I pneumococcus infection, but probably also against Type II.

Results in the Practical Application of Specific Therapy. There is clinical evidence in favor of treatment with Type I antipneumococcic serum in improvement in the patient's general condition, lowered temperature and pulse rate, less mental disturbance, little or no extension of the pneumonic process and a checking of the septicaemia. But judgment is difficult regarding the importance of such apparently favorable indications in the face of wide variations in

the course of the disease in individual patients with lobar pneumonia not treated with serum. There is further evidence of importance in the fact that Felton's anti-body solution is capable of creating a positive balance of protective bodies in the blood of the patient at an early period of the disease when such antibodies are not ordinarily present. The crucial test of the value of specific therapy, however, is its result on mortality.

The most favorable results have been obtained by Cole (Proc. Med. Soc. of the State of N. Y. J. A. M. A. June 30, 1927) in 241 serum treated Type I cases with 24 deaths, a mortality of approximately 10 per cent. Others have been less strikingly successful. A number of factors other than specific therapy, such as the previous condition of the patient, yearly variation in mortality and most important of all, age, may also modify the death rate. Cole estimated the average hospi-

tal mortality for Type I pneumonia at 25 per cent to 30 per cent, but it now appears that it may be considerably lower than his figures. Cecil, Baldwin and Larsen (Arch. Int. Med. Sept. 15, 1927) report 352 Type I cases not treated with serum at Bellevue with 73 deaths, a mortality of 20.7 per cent. These considerations made it desirable to subject the method to a comparison of the mortality in a serum treated series with that in a contemporaneous group not so treated. When this was done by Locke (J. A. M. A. May 23, 1923) the mortality was found to be practically the same in the two series. It is probable that the inauguration of treatment late in the disease in his and other series is responsible for the apparent failure of the method.

Recent reports (Park and Cooper, Antipneumococcus Serum in Lobar Pneumonia, Administration and Dosage, J. A. M. A. Apr. 28, 1928; Rosenblüth, Relation of Bacteremia in Lobar Pneu-

monia to Prognosis and Therapy, Ibid., Bullowa, The use of Antipneumococcic Refined Serum in Lobar Pneumonia, Ibid., and Cecil N. E. J. of Med. — Aug. 30, 1928) of the results with Felton's antibody solution especially when given early in the disease indicate a lowering of mortality in serum treated cases on comparison with a contemporaneous series not so treated.

Our experience (N. E. J. of Med. — Aug. 30, 1928) with the specific treatment of Type I pneumococcus pneumonia treated intravenously with serum embraces 81 cases. Seventy-one were treated with unrefined Type I antipneumococcic serum and 10 with Felton's antibody solution, with 17 deaths, a mortality of 20.9 per cent. The ages in the treated group varied from 5 to 65. The average age was 34.75 years. During the period covered by the serum treated cases, 80 patients with Type I pneumococcus pneumonia, not treated with

serum, were observed, with 19 deaths, a mortality of 23.7 per cent. The ages in this group varied from $3\frac{1}{2}$ to 70 with an average of 37.29. The mortality in the serum treated group on comparison with the controls though suggestive of benefit is so nearly the same as to warrant no definite conclusion as to the value of the method in the series as a whole. Specific treatment is obviously of value only when our results and those of others in early Type I infections are considered.

Results in the early treatment of pneumonia. Of the 81 serum treated cases in our series specific therapy was given in 28 within the first three days of the disease with 2 deaths, a mortality of 7.14 per cent. The ages of these treated patients varied from 12 to 65, the average age being 34.8. Of 21 patients admitted within the first three days and not serum treated 5 died, a mortality of 23.3 per cent. The ages in this group varied from $3\frac{1}{2}$ to 68 with an average of 29.5. The

number of early serum treated cases in the series is too small to warrant any definite conclusion, but in our experience combined with that of others (Table II) 192 patients with Type I pneumococcus pneumonia have been treated with immune serum or its derivatives within the first two to three days of the illness with 21 deaths, a mortality of 10.9 per cent.

The question has been raised whether early admission to the hospital of patients with Type I pneumonia may not of itself lower the death rate, but this can be answered in the negative. Of 168 patients with Type I pneumococcus pneumonia (Table II) admitted within two to three days of the onset, not treated with serum, 44 died, a mortality of 26 per cent. The number of cases and the low mortality in the combined group on comparison with the controls may be taken to indicate curative value in early treatment.

TABLE II. — TYPE I PNEUMOCOCCUS PNEUMONIA TREATED INTRAVENOUSLY WITH HOMOLOGOUS ANTIPNEUMOCOCCIC SERUM OR ITS DERIVATIVES WITHIN THE FIRST FEW DAYS OF THE ILLNESS

		Treated Group				Control Group		
	Days of disease when treatment began	Material	Cases	Deaths	Mortality Per cent	Cases admitted within corresponding Interval	Deaths	Mortality Per cent
Locke, J. A. M. A. May 26, 1923	3	whole serum	12	0	0.0	..	..	..
Christian, Peter Bent Brigham Hospital	3	whole serum	13	2	15.3	..	..	..
Cecil, Arch. Int. Med. vol. 41, No. 3, March. 15, 1928	2	Huntoon's antibody	56	5	8.9	68	16	23.5
Bullowa, J. A. M. A. Apr. 28, 1928	3	Felton's antibody	29	6	21	28	10	36
Cecil, N. E. J. of Med. Aug. 30, 1928	3	Felton's antibody	54	6	11.1	51	13	25.5
Lord, N. E. J. of Med. Aug. 30, 1928	3	whole serum	24	2	8.3	21	5	23.3
		Felton's antibody	4	0	0.0	..	..	..
Totals.....	..	..	192	21	10.9	168	44	26

Advantages of Felton's Antibody Solution. The concentrated material permits the intravenous administration of a potent solution in a small volume. Whereas the unrefined serum was given in 100 cubic centimeter doses, this antibody solution can be given in doses of 5 to 10 cubic centimeters. The antibody is made from the serum of horses inoculated against all three types of pneumococci and is therefore spoken of as polyvalent. It is of established value against Type I pneumococcus pneumonia and is of probable value also against Type II. Unlike unrefined antipneumococcus serum, reactions following the use of the antibody solution are not sufficiently troublesome to make it necessary to determine the type of infection previous to its administration. It can therefore be given at once without waiting for type determination and this means a saving of at least 24 to 48 hours in the inauguration of specific treatment of the dis-

ease. Early adequate dosage may thus be established. No complicated apparatus is necessary. Precautions must still be taken, however, against its use in patients who may be hypersensitive to horse serum.

Precautions in the Use of Alien Serum in Man. Certain precautions should always be used in the administration to man of serum obtained from an alien species such as the horse, and this applies not only to the treatment of pneumonia with antipneumococcus serum but also among other diseases to the treatment of meningitis with antimeningococcus serum, the prevention and treatment of diphtheria with diphtheria antitoxic serum, and the prevention and treatment of tetanus with antitetanus serum. All these sera are made by the immunization of horses and when the resistance of the horse is raised to a sufficient degree the horse is bled. The blood is allowed to clot and the separated

serum removed. The treatment of pneumonia is by the injection of Felton's antibody solution directly into the veins of the patient. The serum used in the prevention and treatment of diphtheria is usually injected under the skin but at times is also given directly into the veins. Antimeningococcus serum is usually given directly into the spinal canal, at times also into the veins. Antitetanus serum is injected under the skin to prevent the disease and both into the spinal canal and into the veins in treatment.

Following the administration of horse serum by any of these routes, certain symptoms of a varying degree of severity may arise in susceptible individuals. These symptoms have nothing to do with the preventive and curative action of the serum but arise in consequence of the entrance directly into the body of serum, containing substances of a protein nature common to the horse but foreign to human beings. Fortunately

only a small proportion of patients are sensitive to horse serum and the susceptibles are easily recognized by certain simple procedures. In the first place the patient under consideration for serum treatment should always be asked whether or not he is subject to or has had hay fever or asthma, or if he has ever previously been given an injection of horse serum and an affirmative answer places him in the group of patients likely to be sensitive to serum, and indicates that special caution should be observed in the use of horse serum. About one-quarter of those who have been immunized against diphtheria by the toxin-antitoxin mixture are sensitized to horse serum. In all candidates for serum treatment, however, irrespective of the response to these questions sensitiveness to horse serum should be tested directly by what is known as an intradermal skin test performed by the injection into and not under the sterilized skin, by means

of a very fine needle, of a small amount (0.02 c.c.) of sterile horse serum diluted (1.10) with normal salt solution. To prevent confusion with a local reaction due to the injection itself, an equal amount of normal salt solution alone is similarly injected into another part of the skin and the two sites of injection are observed. In sensitive individuals there develops at the site of the injection of the horse serum, usually within about five minutes, a peculiar white elevation resembling nettle rash and spoken of as an urticarial wheal and surrounded by a zone of redness. The urticarial wheal slowly increases in size, may reach that of a half dollar within an hour and then slowly subsides while the site of the injection of salt solution presents no such appearance.

In patients without a history of hay fever, asthma, or the previous injection of horse serum, and with negative skin tests, the intravenous administration of

antibody solution may be given. In those with a history of hay fever, asthma or a previous injection of horse serum and with negative skin tests, antibody solution may also be administered, but first subcutaneously in doses of from 0.005 to 0.025 c.c. doubling the dose every half hour until 1.0 c.c. has been given. Intravenous dosage may then be started with 0.1 c.c. and the dose doubled every half hour until the desired amount has been reached. For the present it would seem best not to administer the antibody to those who are skin sensitive to horse serum.

Further experience may show that sensitiveness to unrefined horse serum does not of necessity mean that the individual is sensitive to the antibody solution and it is desirable that this matter be settled by skin tests with the antibody solution in patients found to be skin sensitive to unrefined horse serum.

Administration of Antibody Solution. The antibody solution is usually given into a vein at the bend of the elbow. It should be warm and given slowly, five minutes being spent in giving the first five cubic centimeters. The slow administration is desirable as an added safeguard against sensitiveness to serum, the symptoms of which are likely to occur at once if they are to develop at all. Subsequent doses are given usually at eight or twelve hour intervals while the temperature remains high or septicemia is shown to be present.

Stress has been laid on the precautions which should surround the administration of horse serum and if these precautions are observed no unfavorable symptoms should occur in consequence of the injections. Before leaving the subject mention should be made of three types of reactions which may follow the intravenous use of horse serum.

Reactions following Serum Injections. During or immediately following the injection of serum in sensitive individuals there may develop what is spoken of as a shock-like reaction. The precautions already described are designed to avoid such reactions. When serum is given to sensitive individuals a general urticarial eruption or an asthmatic attack with rapidity and weakness of the pulse may occur. Such an attack may be fatal. Atropine sulphate 1/60 to 1/30 grain and adrenaline chloride, 10 minims of a 1:1000 solution subcutaneously will usually relieve the symptoms.

A second type of reaction which may occur in consequence of serum administration is a rapid rise of temperature which usually occurs within an hour, accompanied by chill or chilliness, some shortness of breath and cyanosis and elevation of pulse. This is called a thermal reaction. The temperature elevation is of short duration and is followed by a

fall frequently to below the previous temperature level. This reaction is rather disturbing to the patient but is not dangerous. Thermal reactions are uncommon after Felton's antibody solution.

A third consequence of serum treatment, more remote in point of time, is what is known as serum disease, which may occur about one week or later after the last injection and may last for a number of days, or a week or more. The symptoms are elevated temperature, urticarial skin rashes, swelling of the skin, stiff and painful joints, and enlarged glands and spleen. This condition though troublesome is not serious. A soothing skin wash and adrenaline chloride solution subcutaneously will give some relief from the itching. Serum disease occurs in only 10–12 per cent of patients after the use of Felton's antibody solution and is usually very mild.

Conclusions

In conclusion let me say that though pneumonia still heads the list of acute diseases most widespread and fatal to mankind and though the problem is not yet completely solved, yet much valuable knowledge has already been gained.

Within recent years important advances have been made in the study of the pneumococcus. Its distribution and mode of transmission are better understood. The pneumococcus has long been known to be a common inhabitant of the normal mouth, as well as the cause of pneumonia, but it has only recently become apparent that all pneumococci are not alike in their behavior as infectious agents. Types I and II, which cause about one-half of all cases of lobar pneumonia are almost wholly confined to patients with pneumonia and to persons intimately exposed to them. This discovery, together with the knowledge

that in general the passage of bacteria through animals increases their virulence, makes it desirable to regard pneumonia as a contagious disease and guard against transfer of the infectious agent from the sick to the well with much greater care than was formerly the custom. The methods of preventing such transfer are already understood and should be much more strictly applied. Conditions of overcrowding are now known to be important in increasing the prevalence of the disease and should whenever possible be avoided.

A most significant advance, capable of saving many lives, has already been made in the treatment of pneumonia due to Type I pneumococcus with antibody solution. The earliest possible administration of the antibody solution is essential for the best results.

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